REMARKS

The following remarks are in response to the Examiner's Office Action mailed on October 31, 2006 and Applicants' interview with Examiner Zachariah Lucas on September 26, 2006. Claims 2, 9 and 23 have been canceled and claims 16–20 withdrawn. Claims 6, 21, 22, and 24 are amended. New claims 27 and 28 are added. Claims 1, 3-8, 10–22, and 24-28 are pending.

I. Interview with Examiner

Applicants express appreciation to Examiner Lucas for conducting a telephone interview with Applicants on September 26, 2006. During the interview Applicants discussed the patentability of claims 1, 3-8, 10–22, and 24-26 in view of Thomas et al. which was published in *Oncogene* on September 6, 2001, vol. 22, pp. 5431-5439, details of which are described in the following sections.

II. Claim Objection

Claims 21 and 20 stand objected to because of informalities. Applicants amend claims 21 and 20 to correct the informalities by reciting "method of claim 1, or 10." Withdrawal of the objection is therefore respectfully requested.

III. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 6-8 stand rejected under 35 U.S.C. §112, Second Paragraph as being indefinite. Applicants amend independent claim 6 to clarify that the claim is directed to a system for the detection of the presence of an oncogenic human papillomavirus (HPV). Withdrawal of the objection is therefore respectfully requested.

IV. Rejection under 35 U.S.C. §103(a)

Claims 1, 3-8, 10-13, 15, 21, 22, and 24-26 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Davis (U.S. Patent No. 5,610,077) in view of Thomas et al. and Bleul (U.S. Patent No. 5,753,233); claim 14 rejected over Davis in view of Thomas et al. and Bleul, and

further in view of Kehmeier et al. (Virology 299:72-87); and claim 24-26 rejected over Davis in view of Glaunsinger et al. and Bleul.

As discussed in the interview, none of the cited references, each alone or in combination, teaches or suggests the claimed method or system for detecting the presence of an oncogenic HPV in a sample by using a PDZ domain polypeptide of less than 1000 amino acids in length and comprising the amino acid sequence of MAGI-1 PDZ domain 2. First, Davis does not teach or suggest detection of an oncogenic strain of HPV, let alone teaches or suggests detection of an oncogenic strain of HPV by using a polypeptide comprising a PDZ domain 2. Second, Bleul merely discusses serum-reactive epitopes on HPV that could be used to detect HPV 18 E6 protein in blood serum.

Thomas et al. was published in *Oncogene* on September 6, 2001. As discussed during the interview and in Applicants' Supplemental Amendment filed on August 18, 2006, Thomas et al. was published *after* the filing date August 3, 2001 of Provisional Application Serial No. 60/309,841 to which the instant application claims priority. As described in the 60/309,841 Applicants demonstrated that a large number of PDZ polypeptides bind to different PDZ ligands (PLs), such as an E6 protein from oncogenic HPV. In the 60/309,841 Application Applicants also demonstrated that because the carboxy-terminus of the E6 protein from oncogenic strains HPV16, 18, and 31 (T-Q-V/L), and 66 (ESTV), match the consensus PDZ binding motif (pp. 87-88), oncogenic strains HPV16, 18, and 31 would bind to a PDZ domain 2 of BAI-1 (or MAGI-1).

As further evidenced in Dr. Peter S. Lu's Declaration under 37 C.F.R. §1.131, the claimed invention was conceived and reduced to practice prior to September 6, 2001, the publication date of Thomas et al. As stated in the Declaration, prior to this date Applicants designed and purchased from commercial suppliers peptides containing the consensus C-terminal sequences derived from various oncogenic strains of HPV, and C-terminal sequences from non-oncogenic strains of HPV. **Table 1** of the Declaration lists the sequences of such peptides with the C-terminal consensus sequences of oncogenic strains of HPV highlighted in bold. Prior to September 6, 2001 Applicants used the G Assays (described in above-referenced application serial No. 10/630,590 at pages 43-46, and in provisional application No. 60/309,841 filed on August, 3, 2001 at pages 32-36) to assess the interactions of peptides (**Table 2**) derived from the C-terminal 19-20 amino acids of E6 proteins from oncogenic HPV types 33, 35, 58, 66 and non-oncogenic type 57. As shown in

Figure 1 of the Declaration, Applicants demonstrated that all four of peptides derived from the E6 protein of oncogenic HPV strains bound MAGI-1 PDZ domain 2 strongly at 1-10 uM peptide concentration. In contrast, the E6 sequence from non-oncogenic HPV type 57 did not bind to MAGI-1 domain 2. In addition, peptides derived from the E6 protein of oncogenic HPV strains 16 and 18 that share the same consensus C-terminal sequence as strains 33, 35, 58 and 66 were later demonstrated to bind to MAGI-1 domain 2. Thus, since the claimed invention is a method or system for detecting the presence of an oncogenic HPV in a sample by using a PDZ domain polypeptide of less than 1000 amino acids in length and comprising the amino acid sequence of MAGI-1 PDZ domain 2, the claimed invention was conceived and reduced to practice prior to September 6, 2001, the publication date of Thomas et al. Thus, Thomas et al. should not be considered as prior art against the claimed invention.

Applicants also amend claim 24 to specify that the fusion protein is made of heterologous domain and a PDZ polypeptide that is less than 1000 amino acids in length and comprises the amino acid sequence of MAGI-1 PDZ domain 2, which is not taught nor suggested by Glaunsinger et al.

In view of the distinct structural and functional differences between the claimed invention and the methods disclosed in the cited references, a prima facie case of obviousness has not been established under 35 U.S.C. §103(a). Withdrawal of the rejection is therefore respectfully requested.

V. Obviousness-Type Double Patenting

Claims 1, 3-8, 10-15, and 24-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1, 3, 4, 8, 9, and 10 of co-pending patent application 10/847,818; and claims 24-26 provisionally rejected in view of claims 1, 3, 4, 8, 9, and 10 of co-pending patent application 10/847,818 in view of Glaunsinger et al.

As discussed during interview, independent claims 1, 6, 10 and 24 as amended are patentably distinct from the claims of 10/847,818 because the instant claims recite "a PDZ domain polypeptide of less than 1000 amino acids in length and comprising the amino acid sequence of MAGI-1 PDZ domain 2." These elements are not present in and are not reasonably suggested by

the claims of 10/847,818. Thus, the claims of these two applications are patentably distinct from each other.

In addition, the instant application has an earlier filing date, July 29, 2003, than that of the 10/847,818 Application, May 17, 2004. Pursuant to MPEP 804 IB1, "[i]f a 'provisional' nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier-filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

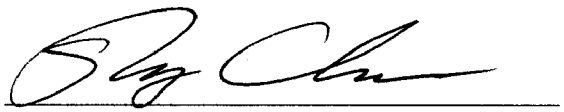
As such, Applicants respectfully request the Examiner to withdraw the nonstatutory obviousness-type double patenting rejection.

CONCLUSION

In light of the amendments and remarks set forth above, Applicants earnestly believe that the pending claims are in condition for allowance, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

The Commissioner is authorized to charge any additional fees that may be required, including petition fees and extension of time fees, or credit any overpayment to Deposit Account No. 23-2415 (Attorney Docket No. 34170-701.501).

Respectfully submitted,

Date: January 31, 2007 By: 

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